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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/659,097	09/10/2003	Rainer Naeff	CCS-202-CON	4324

27777 7590 06/27/2006

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EXAMINER
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VANIK, DAVID L

ART UNIT	PAPER NUMBER
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1615

DATE MAILED: 06/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/659,097

Applicant(s)

NAEFF ET AL.

Examiner

David L. Vanik

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 16 February 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 15-23 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 15-23 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

Receipt is acknowledged of the Applicants' Amended Claims and Remarks filed on 2/16/2006. **It should be noted that this case has been transferred from Gollamudi Kishore to David Vanik.**

As a result of Applicants' amended claims, the 35 U.S.C. 112 first paragraph rejections are hereby **withdrawn**. However, the Double Patenting rejections over US 6,645,522 ('522), the 35 U.S.C. 112 second paragraph rejections, and the 35 USC §103 rejections are hereby **maintained**.

### MAINTAINED REJECTIONS:

The following is a list of maintained rejections:

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 15-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Independent claim 14, as currently presented, is not clear. Specifically, it is not clear whether the EPO is dispersed in the internal (inside the liposome) or external aqueous phases (separate from the liposome) of the composition.

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Although the instant claim 15 discloses that the EPO is "substantially unincorporated within the liposome," this could be interpreted as the EPO not being incorporated into the phospholipids layer of the liposomes. Although the examiner respectfully submits that the instant claim 15 is indefinite, the examiner is interpreting the claim to mean that the EPO is dispersed within the **external** aqueous phase in order to expedite prosecution.

### ***Response to Arguments***

Applicant's arguments filed on 2/16/2006 have been fully considered but they are not persuasive. In response to the 8/19/2005 Non-Final Rejection, Applicant has asserted that the 35 U.S.C. 112, second paragraph rejections over the instant claim set has been obviated by the newly amended claims 15-23. The examiner respectfully disagrees with this assertion. Because the essential elements of claims 15-23 remain unchanged from those examined in the 8/19/2005 Non-Final Rejection, the examiner respectfully submits that the double patenting rejection is proper.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct

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from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 15-23 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,645,522 ('522). Although the conflicting claims are not identical, they are not patentably distinct from each other because, like the instant claims 15-23, '522 claims a liposomal-based composition comprising an aqueous phase comprising an aqueous buffer (such as disodium hydrogen phosphate), a lipidic phase comprising single bi-layered liposomes, and an effective amount of erythropoietin wherein said erythropoietin is dispersed within the external aqueous phase and is substantially unincorporated within said liposomes (See claim 1 of '522). Additionally, like the instant claims 17-23, '522 claim glycine (claim 3 of '522), a preserving agent (claim 6 of '522), an antioxidant (claim 7 of '522), and a complexing agent (see claim 10 of '522). Claims 1-10 of '522 disclose species of the generic liposome-based composition claimed in the instant application. That is, claims 15-23 of the instant application encompass a generic teaching, while claims 1-10 of '522 encompass a specific or species-like teaching. Because '522 claims specific

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compositions comprising a liposomal-based composition comprising an aqueous phase comprising an aqueous buffer (such as di-sodium hydrogen phosphate), a lipidic phase comprising single bi-layered liposomes, and an effective amount a erythropoietin wherein said erythropoietin is dispersed within the external aqueous phase and is substantially unincorporated within said liposomes, one of ordinary skill in the art would have the requisite motivation to claim the generic embodiment of said species. Based on the claims of '522, there is a reasonable expectation that a liposomal-based composition comprising an aqueous phase comprising an aqueous buffer (such as di-sodium hydrogen phosphate), a lipidic phase comprising single bi-layered liposomes, and an effective amount a erythropoietin wherein said erythropoietin is dispersed within the external aqueous phase and is substantially unincorporated within said liposomes would be an effective drug-delivery composition. As such, given the claims of '552, it would have been obvious to one of ordinary skill in the art at the time the invention was made to claim the instant claims 15-23.

### ***Response to Arguments***

Applicant's arguments filed on 2/16/2006 have been fully considered but they are not persuasive. In response to the 8/19/2005 Non-Final Rejection, Applicant has asserted that the obvious-type double patenting rejection over the instant claim set has been obviated by the newly amended claims 15-23. The examiner respectfully disagrees with this assertion. Because the essential elements of claims 15-23 remain

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unchanged from those examined in the 8/19/2005 Non-Final Rejection, the examiner respectfully submits that the double patenting rejection is proper.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 15-16, 19-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over either JP 08231417 or Maintani in view of Collins et al (5,874,075).

JP, and Maitani disclose liposomes containing erythropoietin. The liposome lipids include synthetic lecithin and cholesterol and phosphate buffer (note the abstract of JP; abstract and Experimental section in Maitani). What is lacking in JP and Maitani is the teaching that erythropoietin be on the surface of the liposomes.

Collins as pointed out above, teaches liposomal compositions wherein hematopoietic factors including erythropoietin are attached to the surface of the liposomes. The phospholipids include dipalmitoylphosphatidic acid. The liposomes further contain PEG (stabilizer) and a phosphate buffer. According to Collins, such an attachment stabilizes the proteins such as erythropoietin.

The attachment of erythropoietin on the surface of the liposomes instead of encapsulating it within the liposomes of JP or Maitani would have been obvious to one of ordinary skill in the art since Collins teaches attachment to the surface stabilizes erythropoietin.

### ***Response to Arguments***

Applicant's arguments filed on 2/16/2006 have been fully considered but they are not persuasive. In response to the 8/19/2005 Non-Final Rejection, Applicant has asserted that it would not be obvious to one of ordinary skill in the art to combine the teachings of either JP 08231417 or Maintani with Collins et al (5,874,075). The Applicant asserts that, because both JP 08231417 and Maintani teach liposome-based compositions wherein EPO is incorporated (at least in part) into the liposome, one of ordinary skill in the art would not have the requisite motivation, given the teachings of



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Collins et al (5,874,075), to attach EPO to the surface of a liposome-based composition.

The examiner respectfully disagrees with this assertion.

As currently presented, claim 15 is drawn to a composition wherein EPO is "dispersed within the aqueous phase." As stated above, the examiner is interpreting this to mean that the EPO is dispersed within the **external** aqueous phase. Since liposome-surface attached EPO is present in the external aqueous phase of the composition (as compared to being substantially incorporated into the liposome), giving the instant claim set its broadest reasonable interpretation, the examiner respectfully submits that EPO is dispersed within the external aqueous phase of the composition. The examiner respectfully asserts that there is motivation to combine either JP 08231417 or Maintani with Collins et al (5,874,075) and formulate a liposome-based composition wherein EPO is attached to the surface of said liposome. Specifically, as mentioned in the 8/19/205 Non-Final Rejection, attaching a protein, such as EPO, to the surface of a liposome advantageously stabilizes a protein even under conditions which could denature/destabilize a given protein structure (column 7, lines 26 – 54). Because, as set forth in Collins et al (5,874,075), attaching a protein, such as EPO, to the surface of a liposome can advantageously stabilize said protein even under conditions which could denature/destabilize a given protein structure, one of ordinary skill in the art would have been motivated to attach the EPO protein to the liposome surface of the composition taught by JP 08231417 or Maintani. Based on the teachings of Collins et al (5,874,075), there is a reasonable expectation that the attachment of a protein, such as EPO, to a liposome surface would effectively increase the stability of said protein in an

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aqueous environment even under conditions which could denature/destabilize a given protein structure. As such, it would have been obvious to one of ordinary skill in the art at the time the invention was made to attach EPO to the surface of a liposome in the inventions advanced by JP 08231417 or Maintani in view of the teachings of the increased stability as taught by Collins et al (5,874,075).

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

### ***Correspondence***

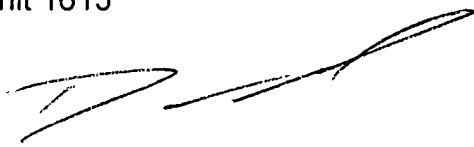
Any inquiry concerning this communication or earlier communications from the examiner should be directed to David L. Vanik whose telephone number is (571) 272-3104. The examiner can normally be reached on Monday-Friday 8:30 AM - 5:00 PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David Vanik, Ph.D.  
Art Unit 1615

  
6/21/06  
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